PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	28 NOV 2006
Applicant's or agent's file reference MSK. P-082WO	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/IB06/51199	18 April 2006 (18.04.2006)	18 April 2005 (18.04.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC: **A61K 39/395**(2006.01), 31/70 (2006.1);**A01N 43/04**(2006.01)
USPC: 424/130.1;514/44

Applicant

SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	12 October 2006 (12.10.2006)	Peter Reddig Telephone No. (571) 272-9031

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB06/51199

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☐ claims Nos. _____

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 6 and 7 are so unclear that no meaningful opinion could be formed *(specify)*:

Claims 6 and 7 are improper multiple dependent claims.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 5 and 11	YES
	Claims 1-4,8-10 and 12	NO
Inventive step (IS)	Claims 5 and 11	YES
	Claims 1-4,8-10 and 12	NO
Industrial applicability (IA)	Claims 1-5 and 8-12	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-4, 8-10, and 12 lack novelty under PCT Article 33(2) as being anticipated by US Pat App. Pub 2003/0224993 (Land et al.) 04 December 2003 (04.12.2003).

Land et al. teach a method of reducing the amount of active a6b4 integrin in cancer cells in a patient by the administration of a therapeutic agent targeted to a6b4 that kills the cancer cells, see para. 0023, 0312-0340, claims 1-16, 24-40, 64-66. Land et al. teach administering the agents to humans in compositions suitable for human administration, see para 0261-0262, and 0340. Land et al. teach that the anti- a6b4 integrin therapeutic agent is an antibody, para 0049-0078. Land et al. teach that the anti-a6b4 integrin therapeutic agent is an antisense oligonucleotide, see para 0048, 0097-0100, claims 27 and 29. Land et al. teach treating breast, prostate, and cervical cancer cells in vivo, see para 0329 and 0340. Land et al. teach administering the ErbB2 inhibitor Herceptin with the anti- a6b4 integrin therapeutic agent, see para. 0313-0314. Land et al. teach that the anti- a6b4 integrin therapeutic agents are used in the preparation of pharmaceutical compositions, see para 0255, 0256, and 0282-0302.

Claims 1 and 3 lack novelty under PCT Article 33(2) as being anticipated by Dajee et al. Nature. February 2003. Vol. 421, pages 639-643.

Dajee et al teach a method of inhibition of tumorigenesis in a mouse tumor model in cells expressing a6b4 integrin by treating with antibodies to a6b4 integrin, see p 640, right column, and Fig. 4C and 4D.

Claims 1-12 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.